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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,422	02/17/2004	Herbert W. Harris	18184-0006 CI1	3052

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	
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10/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,422	HARRIS ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *3-6,10-12 and 16-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-9 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Response to Restriction Requirement Acknowledged

1. Applicant's election, with traverse, with the Group I(a) along with (S)-1-(3',4-dimethoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine and hot flashes associated wit menopause as the elected species is acknowledged. Claims 1, 2, 7-9 and 13-15 read on the elected invention.

Applicant's amendment filed 07/16/2007 now presents claims 22-30 as a linking claim of independent claim 1. As the applicant points out correctly, the amended claim 1 link(s) inventions I(a) and I(b). The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 22-30. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re*

Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Accordingly, claims 3-6, 10-12, 16-20 and 21-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1, 2, 7-9 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 recite "substantially free of the corresponding (R)-enantiomer ". The term "substantially" in claim 1 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale In this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ito et al. (AN 1981:473687, abstract, Iyakihin Kenkyu, 1981, 12(2), 587-600).

Ito teaches the pharmacological effects of tofisopam (racemic mixture), in vivo and in vitro, in inhibiting spontaneous locomotion and acetic acid-induced stretching, decreasing body temperature and elevating pain threshold.

As discussed in preceding comments, the instant invention does not clearly define what is the requisite degree of "substantially free of the corresponding (R)-enantiomer" in said composition. Given "broadest reasonable interpretation" of term "substantially free of the corresponding (R)-enantiomer", the examiner determines that the scope of the invention encompasses tofisopam (which is 50:50 racemic mixture of (S) and (R) enantiomers). Thus, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 7-9 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landry (USP 6,080,736).

Landry teaches the treatment of anxiety and anxiety disorders in a human using optically pure tofisopam. See column 1, lines 11-13. It is also taught that the racemic tofisopam is active in treating anxiety disorders, nervous tension, irritability and disturbed sleep patterns with menopausal symptoms, enhance the action of diazepam against convulsions, tremor, cognitive performance in anxious patients etc. See column 7, lines 36-column 8, line 45. Tofisopam is used in the treatment of symptoms of anxiety disorders such as sweating, palpitations, trembling, hot flashes etc. See column 9, lines 43-47. It is also taught that the stereoisomers of tofisopam show different pharmacological effects in mice and thus different biological activity which does not correspond with the sum of the activities of the individual enantiomers. See column 9, lines 1-10. It is further taught that the racemic mixture of tofisopam causes adverse effects such as excess stimulation, agitation and inability to sleep. The prior art suggests

to use a single enantiomer to reduce adverse effects and thus an improved therapeutic index. See column 15, lines 28-36.

Landry does not expressly teach the administration of S-tofisopam for treating symptoms of anxiety disorders such as hot flashes, sweating, palpitations comprising administering S-tofisopam.

Landry does not expressly teach the method of lowering body temperature comprising administering S-tofisopam.

It would have been obvious to a person of ordinary skill in the art at the time of invention to treat symptoms of anxiety disorders by administering optically pure S-tofisopam because Landry teaches that 1) optically pure enantiomers of tofisopam can be used for treating symptoms such as hot flashes, sweating, palpitations etc., and 2) optically pure tofisopam have different biological activity, and also have reduced adverse effects. One of ordinary skill in the art would have been motivated at the time of invention to administer optically pure S-tofisopam with the expectation of treating hot flashes, sweating, palpitations, convulsions etc., by lowering body temperature, and with reduced adverse effects, associated with racemic tofisopam.

Note: Applicant's disclose that S-tofisopam can be used in treating convulsions and/or seizures in the US Patent 6,649,607, and EP 1 262 184.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed.

Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 2, 7-9 and 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 and 31 of copending Application No. 10/10827839. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '839 Application teaches a method of lowering body temperature comprising administering an S-enantiomer of a compound of Formula I which encompasses (S) tofisopam, while the applicant claims the method of lowering body temperature by administering (S)-tofisopam. Thus it would have been obvious to a person of ordinary skill in the art to administer a composition comprising (S) tofisopam as disclosed in '839 with the expectation of reducing body temperature, thereby treating a disorder associated with an elevated body temperature (e.g., fever, malignant hyperthermia, serotonin syndrome, hot flashes, cerebral ischemia and stroke).

6. Claims 1, 2, 7-9 and 13-15 are rejected under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 7-22 of U.S. Patent No. 6,649,607. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the prior art administering same compounds, in overlapping dosage amounts, inherently possessing therapeutic effect for the same ultimate purpose (e.g., seizure or convulsion) disclosed by the applicant anticipates the claimed invention even absence explicit recitation of underlying mechanism. Thus, it would have been obvious to a person of ordinary skill in the art at the time of invention to lower body temperature by administering S- tofisopam because '607 discloses that S-tofisopam is used for treating convulsions or seizure, and controlling body temperature treats seizures or convulsions.

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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